P44 EXPRESSION OF CALCIUM/CALCINEURIN PATHWAY-REGULATED TRANSCRIPTION FACTOR NFATC1 AND CHROMATIN-REMODELLING GENES BRG1 AND BRM IN INVASIVE BREAST CANCER

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Background: NFATc1 is a transcription factor activated by the calcium/calcineurin pathway, which regulates several physiological processes. Evidence has also shown a role for NFAT transcriptions factors in oncogenesis. BRG1 and BRM are chromatin-remodelling genes that are also regulated by calcium homoeostasis. Diminished expression of BRG1 is associated with poor prognosis in breast cancer, non-small-cell lung cancer, colorectal cancer, and prostate cancer. To understand the biological relationship between these two pathways, we examined the expression pattern of NFATc1, BRG1, and BRM in invasive breast cancer.

Methods: Paraffin blocks of 150 cases of invasive breast cancer were retrieved from Kaiser Permanente Medical Centre database. Monoclonal antibodies against NFATc1, BRG1, and BRM were used, and expression pattern was determined as no expression, weak (1+ staining intensity), moderate (2+), and high expression (3+). Pearson Chi-Squared test was used for statistical analysis.

Findings: NFATc1 was expressed in approximately 22% of the 150 cases of invasive breast cancer, whereas BRG1 was expressed in 56.7% and BRM in 52%. Both nuclear and cytoplasmic expression of NFATc1 was detected, with nuclear expression as the predominant feature. BRM1/BRM are predominantly expressed in the nucleus. Most cases expressing NFATc1 showed 2+ moderate intensity expression patterns. Statistical analysis showed that expression of NFATc1 was highly correlated with the expression of both BRG1 and BRM.

Interpretation: Our preliminary data shows that NFATc1 is expressed in a subset of BRG1/BRM-positive invasive breast cancers. This correlation of two calcium homoeostasis-regulated pathways provides insight into the oncogenesis of breast cancer.

Funding: Kaiser Hospital Foundation Community Benefit Grant.

The author declared no conflicts of interest.

doi:10.1016/j.ejcsup.2011.02.045

P45 INVASIVE FUNGAL INFECTIONS IN HAEMATOLOGICAL MALIGNANCIES AT A REGIONAL CANCER INSTITUTE – ROLE OF PANFUNGAL PCR

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Background: Invasive fungal infections (IFI) vary considerably worldwide and it is difficult to make a definitive microbiological diagnosis. Therefore, we investigated the epidemiology of IFI by use of panfungal PCR (PFPCR), during febrile episodes in patients with haematological malignancies at Kidwai Memorial Institute of Oncology – a Regional Cancer Centre for diagnosis, treatment, and research on cancer in South India.

Methods: Over a period of 11 months, 160 febrile episodes in 125 patients with haematological malignancies undergoing treatment at our institute were prospectively investigated for IFI. Fungal DNA was extracted from whole blood, amplified by PFPCR using primers against the conserved regions of fungal 18SrRNA gene sequences, and speciated by dot-blot hybridisation.

Findings: 30 of the febrile episodes (19%) were positive for fungal DNA, only two of which yielded fungal growth from blood. Frequencies of proven, probable, possible IFI, and fungal DNAemia without radiological or culture evidence were 1.3%, 0.63%, 5%, and 12%, respectively. Infection by *Candida* species predominated (22 of 30 [73%]), of which the majority were *C.albicans* [16 of 22 [73%]). Five of 22 (23%) were due to *C.tropicalis*. Infection due to *Aspergillus* was rare (3%). Using EORTC criteria for defined IFI, the sensitivity, specificity, positive, and negative predictive values of PFPCR were 100%, 87%, 37%, and 100%, respectively.

Interpretation: Although fungal-DNA-positive febrile episodes were seen in 19% of patients, the prevalence of IFI using the revised EORTC criteria was 6.9%. Nevertheless, the high negative predictive value of PFPCR makes it a reliable test that could allow IFI to be excluded in patients with febrile neutropenia, and would render unwarranted empirical antifungal treatment unnecessary.

Funding: Indian Council of Medical Research.

The authors declared no conflicts of interest.

doi:10.1016/j.ejcsup.2011.02.046

P46 ADVERSE EVENTS OF NIMOTUZUMAB COMBINATION THERAPY IN PATIENTS WITH ADVANCED CARCINOMA

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Background: We evaluated adverse events of nimotuzumab combined with chemotherapy, radiotherapy, or chemoradiotherapy in treatment of advanced carcinomas.

Methods: We reviewed 835 patients with pathologically diagnosed malignant tumours of stage II–IV with metastasis, who were treated from January, 2010, until October, 2010, at 40 hospitals nationwide, by nimotuzumab combined with radiotherapy, chemotherapy, or chemoradiotherapy. Generally, patients were receiving a dose of 45–72 Gy radiotherapy. Patients who were also receiving chemotherapy were mainly receiving platinum agents. All patients were receiving 100–200 mg nimotuzumab once a week at the same time as the other therapies.

Findings: Medical records could be analysed in 792 cases, of which 241 were nasopharyngeal cancer (28.86%); the next most common type of malignancy was head and neck cancer (153 cases [18.32%]). Patients were 37–75 years with a median age of 63.

Male-to-female ratio was 5:2. In more than 90% of cases, the pathology was squamous-cell carcinoma. Adenosquamous carcinoma and adenocarcinoma were less than 10%. Cancers staged as IV, III, and II made up 38.2%, 53.7%, and 10.1% of cases, respectively, and 23.6% of cases involved metastasis. 22 patients (2.63%) had adverse reactions that were unlikely to be due to nimotuzumab, including chills and fever in eight cases (0.96%), rash in five cases (0.6%), oral mucositis in three cases (0.36%), gastrointestinal symptoms (vomiting or diarrhoea) in two cases (0.24%), and dizziness in one case (0.12%). One patient had significant fatigue (0.12%), five had thrombocytopenia (0.6%), and five had decreased white blood-cell count. Nimotuzumab-induced allergy occurred in one case (0.12%).

Interpretation: Nimotuzumab combined with chemotherapy, radiotherapy, or chemoradiotherapy for patients with advanced carcinoma is well tolerated and safe.

Funding: China national Twelfth Five-year Program Funds and Beijing Science Plan.

The authors declared no conflicts of interest.

doi:10.1016/j.ejcsup.2011.02.047

P47 CLINICAL OBSERVATION IN NASOPHARYNGEAL CARCINOMA TREATED WITH ANTI-EGFR MONOCLONAL ANTIBODIES FOLLOWED BY HELICAL TOMOTHERAPY

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Background: We evaluated clinical outcomes and acute toxicity in nasopharyngeal carcinoma treated with tomotherapy followed by anti-EGFR monoclonal antibodies.

Methods: Between March, 2008, and November, 2009, 34 patients with newly diagnosed nasopharyngeal carcinoma were treated with helical tomotherapy combined with nimotuzumab (group N) or cetuximab (group C). All patients received tomotherapy at 70 Gy/33F for the gross tumour volume (pGTVnx) and positive lymph nodes (GTVnd), 60Gy/33F for the high-risk clinical target volume (CTV1), and 56 Gy/33F for the low-risk clinical target volume (CTV2). 17 patients in group N were given a weekly injection of 200 mg/m^2 for 6–7 weeks, and 17 patients in group C were given an initial intravenous dose of 400 mg/m^2 in the first week, followed by weekly injections of 250 mg/m^2 for 6–7 weeks. Acute lesions were evaluated with the RTOG/EORTC criteria.

Findings The median follow-up was 22 months. Effective rates (complete + partial responses) at 3, 6, and 12 months were 82.4% (14/17), 70.6% (12/17), and 70.6% (12/17) in group N, and 88.2% (15/17), 82.4% (14/17), and 82.4% (14/17) in group C. 1-year survival was 88.2% (15/17) in group N and 100% (17/17) in group C. Nimotuzumab was associated with less acute mucositis ($u = 2.245$, $p < 0.05$), weight loss ($t' = 2.563$, $p = 0.0153$) and rash ($u = 4.362$, $p < 0.01$) than cetuximab.

Interpretation: Helical tomotherapy combined with nimotuzumab or cetuximab was effective for nasopharyngeal carcinoma, and there was no difference in short-term efficacy or 1-year survival. Nimotuzumab has fewer acute reactions than cetuximab. More studies should be done to ascertain the long-term effects.

Funding: China national Twelfth Five-year Program Fund and Beijing Science Plan.

The authors declared no conflicts of interest.

doi:10.1016/j.ejcsup.2011.02.048

P48 PILOT STUDY OF TARGETED THERAPY WITH EGFR ANTIBODY (NIMOTUZUMAB) IN PATIENTS WITH UNRESECTABLE HEAD AND NECK CANCER

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Background: We explored the efficacy of biological targeted therapy combined with chemotherapy.

Methods: 71 patients (54 men and 17 women; age 30–83 years, mean 60) were enrolled in this study. All patients had locally advanced oral-maxillofacial and head and neck tumours (no indication for surgery or radiotherapy) confirmed by histology and radiology, with indication for biochemotherapy. The chemotherapy regimen given was cisplatin 75 mg/m^2 day 1, paclitaxel 75 mg/m^2 day 1, fluorouracil 750 mg/m^2 days 1–5, and nimotuzumab 200 mg/m^2 weekly.

Findings: Patients completed 2–4 cycles of chemotherapy (mean 2.2). Nimotuzumab was given 2–8 times (mean 4.3). The prognosis was as follows: complete response in four patients, partial response in 39, stable disease in 18, and progressive disease in 3. Seven patients could not be evaluated. The total effective rate, calculated as complete plus partial responses, was 61%. 29 patients had surgery after biochemotherapy. No serious adverse reactions were noted during the course of the treatment, only one case of slight erythra infection.

Interpretation: Nimotuzumab was effective in increasing chemosensitivity and had a good tolerability profile.

Funding: International Technology Cooperation Fund and Beijing Science Plan.

The authors declared no conflicts of interest.

doi:10.1016/j.ejcsup.2011.02.049

P49 ESCALATING WEEKLY FIXED-DOSE OF NIMOTUZUMAB WITH CONCURRENT CHEMORADIOTHERAPY IN PATIENTS WITH ADVANCED OESOPHAGEAL CANCER – A PHASE 1 STUDY

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